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THE PROPHYLAXIS OF NEURO-SYPHILIS

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THE subject of the Prevention of Syphilis of the Nervous System is one of the most fascinating and elusive chapters in the history of modern preventive medicine; fascinating, because we know so much about the virus, and we have within our grasp the weapons for its destruction; elusive, because we possess so little knowledge that is definite to guide us in the utilisation of these weapons.

We have only, for the most part, personal impressions to guide us. Almost everywhere accurate statistical evidence is lacking; research of that particular kind that involves following up cases with adequate controls over long periods of years, perhaps ten or twenty. The work of Fildes, in conjunction with Maitland and Parnell, provides us with most of what we know concerning the earliest changes that occur in the nervous system and cerebro-spinal fluid in early syphilitic infections. Studies like these must form the basis of all future work.

One can, however, emphasise certain paths of investigation which must be opened up by workers in the near future, and one can formulate certain patent conclusions regarding the attainment of our object which arise from what evidence there is at hand.

A. EFFICIENT TREATMENT OF PRIMARY SYPHILIS WHILE THE W.R. IS STILL NEGATIVE IN THE BLOOD

We know that the nervous system is, or may be, affected with greater frequency and at a much earlier stage than was hitherto supposed, so that it behoves the neurologist to concern himself not only with the problem of the established disease and its treatment but with the changes induced in the organism from the time of infection.

The Hunterian sore may be regarded as the first and purely local effort of the host to destroy the invading

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spirochætes. It has been shown that if during the stage of the primary sore spirochætes are injected into the blood stream or subcutaneous tissues, they are rapidly destroyed, so that it would seem at this period that the blood possesses powerful spirochæticidal properties. It is at this time when the patient's immunity is high and the infection limited to the chancre that we can do most to prevent dissemination. Soon the blood loses its spirochætal power and the local defences become overpowered by the parasites, which rapidly invade the general circulation and lodge in every tissue of the body, the nervous system not excluded.

A positive W.R. occurs at the earliest, four to six weeks after infection in the majority of cases. We may regard it as indicating the first expression of a general reaction of the host to the invading organisms. The time elapsing *before* the positive W.R. is of vital importance in the prophylaxis of neuro-syphilis, because it is at this early stage, before there is manifestation of a general infection, that we can hope for a complete destruction of spirochætes. It is, as you know, a mistake, when confronted with a primary lesion, to make the diagnosis of syphilis dependent on a blood test rather than on a dark ground examination for spirochætes. While one waits for the blood W.R. to become definitely positive the spirochætes are intrenching themselves in the nervous and other systems.

It is probably correct for primary sero-negative syphilis when we say with Hoffmann that early or late manifestations are all the more certainly prevented the earlier N.A.B., mercury and bismuth are begun in the primary stage.

The evidence for involvement of the nervous system at this very early stage of the disease rests upon the following points: (1) The finding of the spirochæta pallida in the spinal fluid, in cases of early syphilis, even of patients whose general examination is negative and whose spinal fluids may indeed be otherwise normal. Warthin and Wile found spirochætes in artificially prepared clot from the cerebrospinal fluid in four out of fifteen cases of early syphilis. (2) The further convincing proof afforded by the study of the spinal fluid abnormalities in late primary and early secondary syphilis. I shall return to this later, but possibly it is safe to say that 30 per cent. of all

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syphilitics show early spinal fluid changes, and this percentage is even higher during the stage of secondary manifestations. This statement does not imply that in the other 70 per cent. the nervous system remains free, for if the number of organisms reaching the meninges is small, or if the cells of the host fail to react, it will naturally follow that there will be no sign of nervous infection and the spinal fluid will be normal, although spirochætes may be locked away in the fastnesses of the nervous system. (3) *Clinical* evidence of involvement of the central nervous system may be apparent even in the late primary stages of the disease.

It is eighteen years since Ehrlich gave us the spirochæticide, salvarsan. *Has there been in the salvarsan period a decrease in the frequency of neuro-syphilis?* Has the more efficient treatment of primary syphilis resulted in a reduction in the incidence of neurosyphilis?

It is rational to believe that the incidence should be less, but I hold that no definite statement is possible at the present time. One is dependent on personal impressions rather than on accurate statistical evidence. There are certain indications that neuro-syphilis is less frequent. (1) General evidence of a decline in late neuro-syphilis is found in the statistics of a large insurance company (Metropolitan Life Insurance Company), which, in 1917, showed a rate of 16.6 per 100,000, dropping in 1922 to 13.1 per 100,000. (2) I have investigated the number of cases of tabes dorsalis admitted to the National Hospital, Queen Square, during the last twenty-five years. In the period 1903-1914 they made 7-10 per cent. of the total number of patients in hospital; during the past four years they made only 4-5 per cent. of the total cases in hospital.

Such an investigation is of little value because we have to take into consideration the fact that recently many of the cases receive only O.P. treatment and are not admitted to the wards; many are side-tracked into infirmaries; many are excluded to make room for cases of other disease of recent appearance, *e.g.*, lethargic encephalitis.

What I think we *can* definitely say is that the syphilis of the nervous system seen by the neurologists nowadays is earlier and less severe in its manifestations.

It is a commonplace with every neurologist who sees many cases of neuro-syphilis that cases of late neuro-

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syphilis give a history of little or no treatment of the primary disease. Erb has emphasised it for a decade. I myself observe it every week.

Does efficient treatment of primary syphilis give the patient any guarantee of immunity from neuro-syphilis? While this is probably true for the majority, I should like to draw your attention to one or two cases which have come under my notice.

A case attended my O.P at the West London Hospital complaining of headaches. Complete physical examination revealed a large oval pupil on the right side which did not react to light—nothing else. He confessed to a chancre seven years ago, treated almost the day after it appeared at a well-known V.D. Clinic in London. Treatment had followed the usual course of modern therapy and extended over a period of two and a half years. Five blood W.R. were taken, the last three negative, *i.e.*, he apparently had energetic treatment. His blood W.R. is now weak-positive, and he has the changes in the cerebro-spinal fluid characteristic of cerebral syphilis.

A patient who was under my care at the National Hospital, when I was House Physician there, acquired syphilis four years before admission. He was treated conscientiously with N.A.B. and Hg during the period of his primary sore, and afterwards over a period of three years. The blood W.R. during the next year was twice negative. To-day he shows signs of tabes.

I will not go into the question as to whether such cases are due to a neurotropic virus which attacks the central nervous system from the first, or whether in these cases there is a tissue predisposition, some susceptibility of the patient's nervous system, rendering it particularly liable to invasion by the spirochæte.

To summarise conclusions in this first section of my paper I would emphasise that the prophylaxis of neuro-syphilis would appear generally to depend on effective sterilisation of the patient, if possible before generalisation of the infection has occurred. Efficient treatment of the primary stages must include thorough physical examination and a study of the cerebrospinal fluid, if the examination of the patient is to be complete. "The procedure of lumbar puncture has great importance in the diagnosis of syphilis *per se*; it is indispensable as a guide to treatment and as a guide to cure or arrest."

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By 1915 it was shown conclusively that early neuro-syphilis could be recognised by spinal fluid examination before the appearance of secondaries. It has become apparent that there is no necessary correlation between symptoms and spinal fluid changes, so that a person with every serological evidence of severe neuro-syphilis may have no symptoms in his central nervous system, while one with severe symptoms of pathological destruction of the nervous system may have a normal fluid. The fact *that the spinal fluid in itself may be the sole guide* to an otherwise symptomless and hidden involvement of the C.N.S. has justified that the test should be routine for all cases at the proper time during their course.

The best time for performing the first lumbar puncture is a matter to be settled by syphilologists—probably after the third injection of N.A.B. in order to prevent drainage infection of the central nervous system.

B. RECOGNITION AND INDICATIONS FOR TREATMENT OF LATENT SYPHILIS

Let us first make clear in our minds what we mean by the latent period. The older clinicians thought of it as a quiescent period occurring between the disappearance of secondary and the appearance of tertiary metasymphilitic infections.

With improved methods of examination it is clear that the period is often not one of quiescence. It is rather, as Professor Stokes has said, "a period of high resistance and low visibility with an undercurrent of chronic mild inflammatory change in vital structures and an upper eddy of alternating cyclical relapse and recovery. It is not a state of inactivity or quiescence except in the rare cases where there has been established a perfect balance between the resistance of the host and the virulence of the invader."

It has long been known that syphilis may attack the central nervous system or, more exactly, the leptomeninges, at a very early stage. The frequency with which this occurs has been the subject of a considerable amount of recent investigation, from which it appears that the C.S.F. shows changes during the late primary or

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secondary period in at least 30 per cent. of all cases of syphilis. Fildes, Parnell and Maitland investigated 1,314 cases of syphilis in the primary and secondary stages, and their monograph in the Medical Research Council's Special Report Series is the most complete that we have on the subject. Dujardin, in his book on the C.S.F. published one year later, in 1921, also published a number of valuable observations. In both of these monographs statistics are arranged according to the duration of the disease, and they provide us with information as to what is the period at which meningeal invasion most commonly takes place.

According to Dujardin, the earliest change in the C.S.F. during the primary and secondary stages is an *increase in fluid pressure*. The estimations were made with a manometer in the lumbar region, and no comparisons were made with corresponding cisternal readings, so that it is difficult to put much reliance on his findings. The pressure of the C.S.F. is a very variable thing, altering with the emotional state of the patient, embarrassment of respiration, and so on.

Broadly speaking, the first warnings of meningeal involvement and reaction are an *excess in the number of cells* and a *rise in the globulin content*. The former is the more trustworthy sign. *The W.R. lags behind* as an index of the late parenchymatous extension of the syphilitic process. In the very earliest stages the pleocytosis consists in an increase of very small lymphocytes.

We may divide the primary stage into two periods :

- (1) The period before the blood W.R. becomes positive.
- (2) The period after the W.R. has become positive in the blood.

Fildes and his co-workers examined 144 cases of primary syphilis in the early period and found a pleocytosis of five cells or more in twenty-one cases, *i.e.*, 15 per cent. Dujardin, in a much smaller series of cases (twenty-one), found no definite change in the C.S.F. at this stage.

In the second period of the primary stage, *i.e.*, after the blood W.R. had become positive, changes in the cerebro-spinal fluid are more frequent. Fildes found it in 21 per cent. in a series of 371 cases, Nicolau in 36 per cent. in a smaller series of fifty-one cases, Dujardin in 20 per cent. in a still smaller series of thirty-two cases. This is all before the secondary stage and the occurrence of any cutaneous eruption. So that in about 20 to 30 per cent. of cases of

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primary syphilis we may expect to find definite change in the C.S.F.

A moderate lymphocytosis, *i.e.*, 10 to 50 cells per cubic millimetre, is probably to be regarded as a protective thing—it has been called a meningeal roseola. Some would put the top limit lower. A severe pleocytosis, 50 to 250, is to be regarded as a frank meningitis.

In the secondary stage we may expect, according to Fildes and his co-workers, meningeal reactions to occur in 40 per cent. (512 cases examined during the first eighteen months).

Jeanselme and Chevallier report changes in 50 per cent. up to the twelfth month, the type of cellular reaction in the later cases is different; large mononuclears and plasma cells appear.

I have said that the W.R. in the C.S.F. lags behind. In the late primary stage it is positive in 3 per cent. of cases. In secondary syphilis it is positive in 11 per cent. It is in the late stages of fully developed neuro-syphilis with clinical manifestations that we find excessively high percentages of positive Wassermann reactions in the fluid.

I have already discussed the inferences to be drawn from the finding of lymphocytosis. I should add to this that the presence of large mononuclears and plasma cells indicates a type of disease that is not responsive to treatment.

Globulin.—As an isolated reaction the finding of increased globulin is of no diagnostic value, as it occurs in many inflammatory and neoplastic conditions of the central nervous system. It indicates, when positive, simply that the meninges are no longer intact and that the permeability of the meningeal vessels has been interfered with.

Wassermann.—This, too, I have discussed. It indicates a generalisation of the spirochætal invasion. It is an index of the patient's attempt to immunise himself against an invading parasite, an immunity which increases with the chronicity of the process. Here again I would emphasise that syphilis of the central nervous system may be progressive to a fatal result with a negative W.R., even in acute cases.

With regard to the *W.R. in the blood*, one would hesitate to draw conclusions from the result of a blood test as to the progressive or innocuous character of a given syphilitic infection.

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Do these fluids, then, that are found to be abnormal in the absence of clinical symptoms of involvement of the C.N.S. pass over into established neuro-syphilis? Here, again, there are gaps in our knowledge. The syphilologist, as Nonne said, never sees the outcome of many of his moves, for the patient reaches the neurologist, whose view-point is, unfortunately, often from an entirely different angle. Dreyfus points out that a certain number of positive fluids again become normal either spontaneously or as the result of treatment. Moore points out that the percentage of patients found to have early spinal fluid abnormalities approximates to the incidence of late clinical neurosyphilis. The incidence of late neurosyphilis, according to most workers, agrees with the figures given by De Brisay and Stokes—44 to 51 per cent. (in a summary of 413 treated and untreated cases).

This percentage approximates to the percentage of abnormal fluids found by Fildes and others in early symptomless involvement of the nervous system. It is certainly true for acute syphilis of the C.N.S., and probably true for late syphilis that the changes which are at first latent in the C.S.F. in many cases pass over into neurosyphilis.

Is the normality of the C.S.F. any guarantee for the future? We used to think so; now we know that we must be cautious and look on it with suspicion. I do not regard one normal fluid as giving the patient this assurance. I saw last week at Guy's Hospital with Dr. Symonds a man of twenty-five complaining of tingling in the two ulnar fingers of the left hand and wrist. There was occasional soreness above the left nipple. The discomfort was continuous and had been present for some months.

Physical examination revealed no weakness, no objective signs, but the distribution of pain and numbness was that of the first, second and fourth thoracic roots—too wide for a cervical rib. He confessed to a chancre five years ago. Four days after the chancre appeared he attended the V.D. department of a London hospital and treatment with N.A.B. and mercury was commenced that day. He attended regularly for treatment over a period of three years, his record card shows his conscientious attendance. In all he had seven blood tests, the last four negative. One C.S.F. examination was made at the end

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of treatment. It was found to be *normal* and he was pronounced cured. He was not told to come up again for control.

Some months ago he married and now has a child. The blood W.R. is now weak positive, the C.S.F. shows a lymphocytosis of 120, globulin plus, a leutic Lange curve and a positive W.R. He has a syphilitic meningitis.

The answer to our question must be "No," if we take as the standard of cure one normal C.S.F. at the termination of treatment. The lesson it teaches is that long controls are imperative in evaluating cure of syphilis.

We know that certain changes in the C.S.F. may persist for years without any subjective or objective signs of nervous involvement. Nonne has observed such cases over as long a period as two and a half years, with examination of blood and fluid as often as eight times. These patients have remained healthy.

Kyrle similarly in Vienna, where there is State control of prostitution, has examined the fluid of luetic women, many of them showing asymptomatic changes in blood and C.S.F. Many of these cases go on for years without subjective or objective signs of nervous involvement.

One occasionally meets amongst the more intelligent class of patients a man who knows he has positive reactions. He observes his pupils and his tendon jerks; he asks about infection of his wife and child. He hears that the Benzoin curve is more reliable than the Lange reaction. His fluid still remains positive after various methods of treatment. He gets depressed and hypochondriac. If he is untreated he will believe that he is being neglected, or ignored, and he will go to a neurologist or syphilologist whom he knows to be more active. If you treat him, and he knows he is being treated by the most modern therapeutic measures, and his isolated spinal fluid reactions remain refractory, as probably they will, he becomes more and more depressed and begins to believe that his disease is incurable.

It is often wise to give such a patient a rest and treat his mental condition for a time, bearing constantly in our minds that such persistent positive reactions are, in my own experience at any rate, commonly of evil omen. They portend future relapse. If the blood is positive in latency after efficient treatment it will probably remain so, even after further treatment. Let us desist for a while

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from specific therapy, watching the fluid for indications for further treatment.

When we stumble on a case which has been *insufficiently* treated in the early stages, and we find positive reactions in fluid or blood, it is time to treat energetically. There will in most cases be an improvement in the reactions, which must be controlled by further fluid examinations.

SUMMARY OF PROPHYLACTIC METHODS IN THE LATENT STAGE

(1) Advise examination of the fluid in all cases of latency. One normal fluid at the end of treatment is not sufficient proof of cure. The frequency of C.S.F. examination cannot be made a matter of rule. The consultant may frighten the patient by emphasising such a disagreeable ordeal as a lumbar puncture. A biennial complete examination, including a physical and neurological overhaul, is a fair compromise. This should extend over a period of ten to fifteen years.

(2) When the C.S.F. is normal let the case alone, but control it *provided the patient has had efficient treatment*.

(3) When the fluid is positive treat energetically with all means at our disposal.

(4) When fluid reactions remain positive in spite of energetic treatment, search for disease, give specific treatment a rest, but watch the C.S.F.

While it is possible at this stage of our knowledge to draw up certain rules regarding the treatment of latent syphilis involvement of the nervous system, we must, however, realise that we are still unable to tell how an individual case is going to react to treatment. The frequency of the stirring up of a latent case by N.A.B. is probably not great, but a case has fallen within my own practice which is of interest in this connection.

The patient was a man of forty-eight years, who developed syphilis at the age of nineteen years in the pre-Wassermann days. He was efficiently treated with mercury and iodide over a period of five years, and at the end of this time he had the permission of two consultants to marry. He married, and his wife remained healthy and he had two healthy children. Two years ago he had occasion to consult a neurologist for what turned out to

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be a non-neurological complaint. The neurologist had his blood tested. The W.R. was found to be positive, and he was advised treatment with N.A.B. After the fourth injection the patient suddenly developed headache, lateral nystagmus, paræsthesiæ on the left side of the face, and left nerve deafness. The nystagmus, paræsthesiæ and nerve deafness have remained.

Nonne describes a closely similar case, where bilateral nerve deafness developed in a patient with latent syphilis during a course of N.A.B. injections. The damage was serious and permanent. He remarks that *deafness due to N.A.B. is unknown*. Such cases must be considered as a flare-up of meningeal syphilis and should probably be classified as Herxheimer reactions. "They are hardly to be regarded as neuro-recurrences in the strict sense, though expressive of kindred neuro-syphilitic lesions."

C. ABORTIVE TREATMENT OF EARLY SYPHILIS OF THE NERVOUS SYSTEM

The incubation period of clinically manifest syphilitic disease of the nervous system ranges from three months to over twenty years. If we make a graph of it we see a rise during the first year due to acute syphilitic meningitis, meningomyelitis and cerebral syphilis. There is a further rise six to eleven years later due to the fact that tabes and G.P.I. have their greatest incidence at this period of time after infection. Thus the conception has arisen of *Acute Syphilis of the Nervous System*—a virulent process where the patient's resistance is relatively low, and *Chronic Syphilis of the Nervous System*—characterised (1) by the mildness of the early lesions; (2) the long latent period, indicating a high degree of resistance in the host; (3) the chronicity of the commoner forms (tabes and G.P.I.); and (4) the absence of signs of acute constitutional reaction, *e.g.*, fever.

This view brings into line the long incubation periods sometimes seen in congenital neurosyphilis. The children who are born alive and live apparently in a healthy state for ten to twenty years or longer before they show signs of nervous disease are those who have acquired immunity during the period of gestation and maintain it subsequently.

Those who die soon after birth or prematurely are those

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who have acquired no such immunity and in whom the syphilitic disease is acute and fatal.

The *pathological unit* which concerns us in syphilis of the nervous system is the group of lymphocytes and plasma cells which forms as an irritative reaction about the spirochætes in the perivascular lymph spaces. The reaction set up in the vessels in the form of endarteritis obliterans reduces the blood supply to the parenchyma with ensuing degeneration. The lymphocytic infiltration is gradually replaced by fibrous tissue and further loss of the parenchyma results. The end therefore is a degenerative process. All the time there is multiplication of organisms in local foci, reaction of tissues, suppression of organisms and relapse and redistribution of spirochætes *via* the blood stream and so on.

The pathology of syphilis of the meningeal vessels was first described by Steenberg, a Dane, in 1860, and later in more detail by Heubner in 1874.

Much work has been done recently with regard to the relationship of the two processes, the meningeal vascular and the parenchymatous, exemplified in such a disease as tabes dorsalis.

Nageotte first showed that the primary lesion in tabes was a lesion of the posterior nerve root between its entrance into the cord and the posterior root ganglion. This portion of the nerve is now known as the "radicular nerve of Nageotte," as a tribute to his work. Here one finds in early tabes frequent evidence of the formation of granulation tissue. There is a small pocket of pia-arachnoid on the posterior aspect of the nerve root as it pierces the dura, and here spirochætes lodge.

There is a pocket near the emergence of the anterior root from the dura, but it is not so large. In these pockets the spirochætes collect and provoke the typical reaction.

One or more roots may be affected, and the lesions may be symmetrical or asymmetrical. On the basis of this view the posterior column lesions are secondary to the root lesions. Similar lesions, *i.e.*, granulation tissue in a meningeal pocket, may be found in certain cranial nerves, *e.g.*, trigeminal and oculomotor.

Schaffer and his pupil Richter, in 1920 and 1921, demonstrated spirochætes in these little masses of granulation tissue, and they showed that there was at the same time an endo-radicular process in the lymph spaces within

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the parenchyma of the nerve root. The two processes were not necessarily concomitant; the endo-radicular process might exist without the peri-radicular meningeal one, *i.e.*, meningitis is a frequent but not constant concomitant of tabes. Clinically this is well established.

At the beginning of the disease the short posterior fibres, those in the so-called band of Pierret (a lateral band which terminates in Clarke's column), degenerate. Later the degeneration becomes more general, and the long ascending fibres carrying deep sensibility degenerate throughout the posterior columns.

Speaking generally, with modern methods of treatment we can do much to abort syphilis of the meningeal type. The presenting symptoms in such cases are those of meningeal irritation—headache, a slight change in temperament, mistiness of vision, diplopia, weakness of eye movements, pins and needles of root or cranial nerve distribution, or root pains. There may be *nothing* to be made out on objective examination. We must not expect loss of deep sensibility or absent tendon reflexes. In such cases I would emphasise the value of a positive history of syphilitic infection.

The curability of such cases is probably as high as 80 to 90 per cent. With established disease of the parenchyma it is different.

Ætiology of Neurosyphilis.—There are certain considerations other than pathological which merit consideration from the point of view of prevention. Are there other influences at work in the production of neurosyphilis? *e.g.*, the influence of age, of alcoholism, of trauma, of neuropathic heredity, of occupation, of strain, of mental fatigue.

One takes the view that these are only of importance in so far as they affect the general tissue resistance of the host. They probably play the same part as they do in any other chronic infection, such as tubercle. Eulenburg stated that the earlier in life syphilis was acquired the longer was the incubation period; and with increasing age the length of incubation shortened. This may be true in a very general way only for late neuro-syphilis.

One does not believe that tabes or G.P.I. are ever produced by trauma, or that brain-workers are more liable to cerebral types of neuro-syphilis than to spinal. Nonne, however, believes that alcoholism predisposes to

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cerebral syphilis, and he points out that the syphilis of alcoholism is a syphilis gravis. Tarnowsky has published statistics of 100 cases of cerebral syphilis showing that not less than forty-three were habitual drunkards.

D. THE PROBLEM OF THE SYPHILITIC PARENT

A meagre estimate of the number of syphilitic husbands who will develop neuro-syphilis may be put at 5 to 10 per cent. The whole question of marriage and syphilis has been fully discussed at this Society already, and I do not intend to go over the ground again.

The question centres largely on two points :—

- (1) The duration of infectivity of syphilis ; and
- (2) The sex of the patient.

While it is easy to lay down rules of fitness for marriage, it is vastly more difficult to induce acceptance of such theoretical requirements in practice. It is a very practical fact that the majority of patients will give little consideration to rules when they have made up their minds to marry.

Summarising the points that will guide us we must take into consideration :—

(1) *The Duration of the Disease.*—In latent syphilis we must regard infectivity as still being present, and a long experience has indicated that the danger lies in the first five years. *The Hoffmann rule*, which crystallises conservative European opinion, calls for three years of treatment with N.A.B. and mercury and two years of symptom-free observation before marriage. In the light of modern work this would include a repeatedly negative blood and C.S.F. from the end of the first six months of treatment. At the end of the fifth year a thorough physical examination is necessary, and integrity of the central nervous system and cardiovascular system proved as far as possible.

(2) *The Sex of the Patient.*—Women being far less eligible than men.

(3) *The Course of the Infection.*—Those with early involvement of the central nervous system and those with fixed positive reaction being judged usually unfavourably.

(4) *The Amount of Treatment*—which should have met the approved requirements of the present day.

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(5) *The Economic Status* of the contracting parties (Stokes).

If marriage is undertaken during the infective period it is a matter obviously of considerable risk. Stokes has outlined a system of what he calls " Protected " marriage in such cases.

Conjugal Neuro-syphilis.—All combinations of conjugal neuro-syphilis are to be found in the literature. I myself have seen conjugal G.P.I. and G.P.I. with tabes, taboparesis and cerebral syphilis. All the other forms may be found, however.

One is struck, in neurological practice, with the tendency of familial neurosyphilis to breed true. I can recall a family in which the father died in an asylum of G.P.I., the mother was under my care for tabes, and of the younger members of the family, two suffered with choroido-retinitis and one had juvenile tabes.

In Frohlich's series of cases of congenital paretics 16 per cent. of the parents had paresis and an additional 13 per cent. had other forms of neurosyphilis, *i.e.*, 30 per cent. of the parents of juvenile paretics suffered with neurosyphilis. My own experience leads me to believe that the incidence of neurosyphilis in several members of syphilitic families is quite as high as this if one is careful to investigate other members of the family from this point of view.

I showed last year at this Society five cases of congenital paresis in different families occurring between the ages of eighteen and twenty-five years, all of whom had brothers or sisters suffering from neurosyphilis, many of whom were in asylums or had died in asylums. In two cases out of the five one of the parents suffered from a form of neurosyphilis, and, as Dr. Nabarro remarked at the time, symptoms of visceral syphilis were strikingly lacking in the children. This may be interpreted as being the result of an inherited weakness of the nervous system in an individual family to invasion by the spirochætes, or it may be taken as evidence for the existence of a neurotrophic virus with a specific malignancy for the central nervous system.

The Prophylaxis regarding Children.—This embraces the consideration of four points :—

- (1) Birth control.
- (2) Artificial termination of pregnancy.

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- (3) Treatment of the infected mother during pregnancy.
- (4) Examination for existing disease, latent or manifest, in other members of the family and treatment.

With regard to birth control I am convinced that contraception should always be advised when there is a knowledge of previous syphilis in the parents. With regard to interference with pregnancy in the infected mother, from her standpoint, the carrying of pregnancy to term is a reinforcement of her defence mechanism. Pregnancy is treatment for syphilis in the mother. Moreover, treatment of the mother during pregnancy protects the child in so large a proportion of cases that it seems unjustifiable in most to terminate pregnancy.

With regard to reduction of syphilis in the new-born by treatment of the pregnant woman, we have definite statistical evidence of the efficacy of the procedure from the point of view of the mother and the child.

Detection of congenital syphilis in a member of a family should be an indication for a detailed examination, both clinical and serological, of all the others. The controls of blood W.R. and C.S.F. should be those of latency in general. An early fluid examination serves to lend direction to treatment. In no case should a child pass the third year or be sent out for adoption without such a test. It should be repeated at least by the seventh year and probably once afterwards.

Problems of latency in the congenital forms of neuro-syphilis do not differ from those of latency in acquired neuro-syphilis. It is by a closer study of the latent period and its more effective treatment that we can achieve a lessened incidence in congenital neuro-syphilis and congenital syphilis in general—a field offering some of the most wonderful possibilities in the territory of modern preventive medicine.

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